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Prevalence and predictors of adverse reactions in plateletpheresis donors with the perspective of donor safety in a tertiary care hospital of Northern India

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Abstract:

BACKGROUND: Plateletpheresis procedures are generally safe and associated with low adverse reactions. Although donor reactions and injuries are self-limited events, they may discourage donors from future platelet donations.

AIM: The purpose of this study was to determine the prevalence and predictors of adverse donor reactions in plateletpheresis donors, which could serve as targets for interventions to reduce reactions.

MATERIALS AND METHODS: The study included 106 platelet donors over a period of 2 years. The demographic, biometric, and clinical parameters were noted. The data were analyzed for predictors of adverse donor reactions.

STATISTICAL ANALYSIS USED: The data were analyzed using independent sample *t*-test to correlate donor variables such as gender. To correlate other variables such as age, weight, and whole blood processed, Chi-square test was used.

RESULTS: A total of 106 plateletpheresis donations were performed and 13.2% of vasovagal reactions were observed. The significant predictive factors for reactions were young female donors with low body weight in which more than 2.5 L volume of whole blood was processed and more than 250 ml of acid, citrate, and dextrose-A was infused and with single venous access procedures.

CONCLUSIONS: The results of this study are encouraging and helpful in identifying donors at risk for developing adverse reactions during plateletpheresis so that proper and close observation during and after donation as well as timely intervention can prevent most of the unpleasant events of plateletpheresis donors.

Keywords:

Citrate anticoagulation, plateletpheresis, random donor platelet, single donor platelet

Introduction

The term apheresis has its roots in the Greek language, meaning "to remove" or "take away."[1] Plateletpheresis is a procedure where the whole blood is processed from a donor and the platelets alone are separated called single donor platelet (SDP) and the remaining blood components are returned back to the donor.[2] Platelets are used in various clinical settings; their principal therapeutic role is to treat acute hemorrhage caused by thrombocytopenia and to provide prophylaxis from hemorrhage during the

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phase of bone marrow aplasia for oncology patients.[3] A routine plateletpheresis procedure usually takes 1–1.5 h. The product is prepared in a closed automated system and can be stored for 5 days. Routinely, a number of platelets in an apheresis product are equivalent to 6–8 random donor platelets (RDPs).[4] At present, platelet donation is considered to be a safe procedure. For most of the donors, procedure of platelet donation is simple, safe, and without complications, but sometimes, adverse reactions may occur. The adverse blood donation reactions are defined as "any physical or psychological abnormality which a normal healthy donor experiences before, at the time of, or after phlebotomy."[5]

There are several reasons for the increasing preferential use of apheresis platelets over the last 10–15 years. SDP has numerous advantages over RDP which include decreased risk of transfusion-transmitted infections, bacterial contamination, and alloimmunization due to reduced donor exposure.[6,7] In addition, the demand for apheresis platelets has increased in many areas as clinicians have realized that these products might offer medical advantages to their patients. Platelet alloimmunization occurs in patients receiving chronic transfusion support and may cause substantial difficulty in providing patients with platelet components that are clinically efficacious. There is some evidence that the likelihood of alloimmunization depends on the number of transfusions received, and one of the strategies advocated for the prevention of alloimmunization has been to limit the number of donors to which the patient is exposed. Such a goal can be accomplished by transfusing less often or, alternatively, by providing apheresis platelets as the platelet component of choice.[1]

Thus, with the trend toward maximal utilization of platelet donors in the present scenario of decreasing donor pool and expanding usage, this study is planned to review adverse donor reactions and factors predicting them.

Materials and Methods

This prospective study included 106 platelet donors, who were coming for donation to the Transfusion Medicine Department of Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow. A total of 106 plateletpheresis procedures were performed on eligible donors (18–60 years) after taking informed consent. The donor characteristics were uniform as far as possible in the study and as per the guidelines laid down by the Drugs and Cosmetics Act, 1940 of India. There are three categories of plateletpheresis donors at our center, namely first time replacement, first time voluntary, and repeat voluntary. There were certain machine-related and donor-related factors kept in mind before allocation of the donors for plateletpheresis procedure on different machines, such as availability of a particular machine at that particular time, availability of plateletpheresis kit, urgency of the need of the component for the patient, venous access, and donor's body weight and blood volume. Hence, it is practically impossible to uniformly distribute the donors on various machines. However, all necessary and possible steps were taken to maintain the uniformity as far as possible. The adverse reaction rates were compared by appropriate statistical methods accordingly.

All procedures were performed under prophylactic calcium (250 mg) orally. A number of procedures performed on different machines were Fenwal Amicus Separator, version 2.5 (Baxter Healthcare Corporation, Deerfield, IL, USA): n = 43; Fresenius separator (COM.TEC), version 4.00.xx (Fresenius Hemocare GmbH, Bad Homburg v.d.H., Germany): n = 41; and Haemonetics MCS + separator (Haemonetics Corporation, Braintree, Massachusetts, USA): n = 22.

All procedures were performed following departmental standard operating procedure using closed system plateletpheresis kits and acid, citrate, and dextrose-A (ACD-A) as an anticoagulant in the proportion of 1:9–1:12. The end point of each procedure was based on target yield of 3×10^{11} platelets per unit, maintaining blood flow rate of 50–80 ml/min. None of the machines had in-line leukoreduction filters. Donor's demographic details such as age, gender, and plateletpheresis procedure details such as blood volume processed, amount of anticoagulant used, and time taken were recorded. All the procedures were performed under constant supervision of medical staff, and full attention and psychological support were given to each donor. After 5 min of completion of the procedure, local dressing was applied on antecubital area. In postdonation period, donors were kept under supervision for another 20–30 min.

Statistical analysis

All the data were analyzed using computer software IBM-SPSS Statistics, version 13 (IBM Corp., Armonk, NY, USA). The data were analyzed using independent sample t-test to correlate donor variables such as gender. To correlate other variables such as age, weight, and whole blood processed, Chi-square test was used. Odds ratio was calculated to identify variables associated with increased likelihood of donor reaction in plateletpheresis donors. The differences were considered significant when $P \leq 0.05$.

Results

A total of 106 plateletpheresis donations were performed including 99 male donors and 7 female

donors. Out of 106 donors, 80 (73 males and 7 females) donors were donated platelets for the first time and the remaining 26 (all male) were repeat donors. Twelve (12%) male donors had reactions, whereas 2 (28%) female donors had reactions and all were underwent plateletpheresis procedure for the first time. No repeat donors had vasovagal reaction (VVR) in the study. Adverse reactions were more common in females and were more in donors with <60 kg of weight ($P < 0.05$) [Table 1]. On Haemonetics, 6 (27.3%) donor reactions were observed. On Fresenius-single needle (SN) and Fresenius-double needle (DN), a number of reactions were 2 (18.2%) and 3 (10%), respectively. Similarly, on Amicus-SN and Amicus-DN, a number of reactions were 1 (7%) and 2 (6.8%), respectively [Table 2].

Table 1: Donors' (plateletpheresis) demographic details (*n*=106) and comparison of reactors (*n*=14) with controls (*n*=92)

Variables	Controls (%)	Reactors (%)	Overall total (%)	*P*
Total number	92 (86.8)	14 (13.2)	106 (100.0)	
Gender				
Male	87 (94.6)	12 (85.7)	99 (93.4)	<0.001
Female	5 (5.4)	2 (14.3)	7 (6.6)	
Age (years)				
<20	12 (13.0)	3 (21.4)	15 (14.2)	0.556
20-29	26 (28.3)	6 (42.8)	32 (30.2)	
30-39	35 (38.0)	4 (28.6)	39 (36.8)	
40-49	16 (17.4)	1 (7.2)	17 (16.0)	
>50	3 (3.3)	0	3 (2.8)	
Body weight (kg)				
<60	12 (13.1)	9 (64.3)	21 (19.8)	<0.001
>60	80 (86.9)	5 (35.7)	85 (80.2)	

Table 2: Adverse donor reactions on different cell separators

Cell separators	Platelet procedures	
	Total (*n*)	Reaction (%)
Haemonetics	22	6 (27.3)*
Fresenius-SN	11	2 (18.2)
Fresenius-DN	30	3 (10)*
Amicus-SN	14	1 (7)*
Amicus-DN	29	2 (6.8)*
Total	106	14 (13.2)

*Donor reactions were significantly higher on Haemonetics in comparison to Fresenius-DN and Amicus single and double needle. SN=Single needle, DN=Double needle

Fourteen (13.2%) VVRs were observed, and majority of VVR were mild 11 / 14 (78.6%) in nature. Out of these 14 donors, 12 donors also developed citrate-related reactions, 75% had mild, and the rest 25% donors had moderate citrate toxicity, but none of the donors had severe citrate toxicity [Table 3]. The rate of reaction was higher in the donors in which more than 2.5 L of whole blood was processed, but difference was not statistically significant ($P > 0.05$). The rate of reaction was higher in donors with ACD infusion more than 250 ml ($P < 0.05$) [Table 4]. To identify any association of various factors with the probability of donor reaction, odds ratio was also calculated for profiling "at-risk" platelet donors [Table 5].

The significant predictive factors for adverse reactions were young female donors with low body weight in which more than 2.5 L volume of whole blood was processed and more than 250 ml of ACD-A was infused and with single venous access procedures.

Discussion

Common and uncommon blood donor reactions and injuries can result from plateletpheresis donation. Since red cells are not depleted and the volume lost is routinely replaced with intravenous solutions, the incidences of hypovolemic reactions are lower than whole blood donation.[8] These reactions and injuries are usually transient and self-limited. In very rare exceptions, a donor may sustain permanent damage. These reactions are unpleasant for donors, complicate collection process, decrease chance of obtaining a full unit of SDP, require treatment and monitoring of donors, and are a significant disincentive for repeat donation.

In our study, the incidence of VVR was 13.2%. The adverse reaction rates in various studies were ranging from as low as 0.68% to as high as 16% in plateletpheresis donors.[9,10] This wide variation in adverse reactions during plateletpheresis might be due to the use of newer generation of apheresis machines, DN, and continuous flow method, using smaller extracorporeal blood volume, thus minimizing the risk of hypovolemic effects. The reaction rate was significantly higher in female donors as compared to

Table 3: Grading of vasovagal reactions and citrate toxicity in plateletpheresis donors

Grade	Mild	Moderate	Severe
Signs and symptoms	Anxiety, nausea vomiting, bradycardia, perspiration, hyperventilation, weakness, and hypotension	Loss of consciousness or recovery period is >15 min	Tetany, convulsions, incontinence, or cyanosis with or without syncope
Vasovagal reactions (*n*=14), *n* (%)	11 (78.6)	2 (14.3)	1 (7.1)
Signs and symptoms	Perioral and peripheral paresthesia, chills, shivering	Light-headedness, muscle cramps, nausea, vomiting	Laryngeal spasm, seizures, arrhythmia, prolonged QT-interval
Citrate toxicity (*n*=12), *n* (%)	9 (75)	3 (25)	Nil

male donors (28% vs. 12%). Tomita *et al*. and Yuan *et al*. also observed a significantly higher reaction rate in female donors.[11,12] The higher incidences of reaction in women were related to lower blood volume, with a resulting greater percentage of blood being within the extracorporeal circuit. This resulted in a greater drop in blood pressure during collection leading to more vasovagal reactions. The reaction rate was significantly higher in the group of donors belonging 50–60 kg. Yuan *et al*. also observed a similar finding that donors with low body weight were more prone to adverse reactions.[12] In plateletpheresis, irrespective of body weight, sequestration of blood in extracorporeal circuit is similar. Therefore, donors with less weight and blood volume are more susceptible to hypovolemia.

Table 4: Relation of adverse reactions with whole blood processed and with acid-citrate-dextrose infusion among plateletpheresis donors

Variables	Donor	Reaction (%)	*P*
Whole blood processed (L)			
<2.5	62	4 (6.25)	0.148
>2.5	44	10 (22.72)	
ACD infusion (ml)			
<250	78	5 (6.4)	0.048
>250	28	9 (32.2)	
Total	106	14 (13.2)	

ACD=Acid-citrate-dextrose

Fully automated cell separators are available nowadays based on the principle of centrifugation having either continuous or intermittent flow technology. This study compares three cell separators used in our center. The maximum adverse reactions (27.3%) were observed on Haemonetics, whereas the least (6.8%) reactions observed on Amicus-DN. The reaction rate was also higher with SN procedures in comparison to DN (6.8% vs. 18.2%). The variation in reaction rate on different machines may be due to different donor safety profiles in terms of fluid replacement and programmed safety variables such as the maximum amount of fluid shift allowed, type of method, i.e., SN or DN, or using intermittent or continuous flow technology. DN continuous flow technology extracted lower extracorporeal blood volume and thus probably associated with less vasovagal reactions. In a study by Bueno, the rate of vasovagal reaction seen with procedures performed on Trima Accel (TA) was four times higher than those on Amicus because latter machine routinely provided donors with saline replacement.[13] The rate of reaction was significantly

Table 5: Donor reactions and odds ratio by donor characteristics compared to donors without reactions in plateletpheresis donors

Variables	Donations with reactions (%)	Donations without reactions (%)	Total number (%)	Reaction rate (%)	OR (95% CI)
Overall (*n*)	14	92	106	13.2	
Age group (years)					
<20	3 (21.4)	12 (13.1)	15 (14.2)	20	1.81 (0.44-7.47)
20-29	6 (42.8)	26 (28.2)	32 (30.2)	18	1.90 (0.60-6.02)
30-39	4 (28.6)	35 (38.1)	39 (36.7)	10.2	0.65 (0.18-2.23)
40-49	1 (7.2)	16 (17.3)	17 (16.1)	5.8	0.44 (0.05-3.62)
>50	none	3 (3.3)	3 (2.8)	-	-
Gender					
Male	12 (85.7)	87 (94.6)	99 (93.4)	12.1	0.34 (0.06-1.97)
Female	2 (14.3)	5 (5.4)	7 (6.6)	28.5	2.90 (0.50-16.64)
Body weight (kg)					
50-60	7 (50.0)	14 (15.2)	21 (19.8)	33.4	5.57 (1.69-18.35)
61-70	6 (42.9)	50 (54.4)	56 (52.8)	10.4	0.63 (0.20-1.96)
>70	1 (7.1)	28 (30.4)	29 (27.4)	3.5	0.17 (0.02-1.41)
Different apheresis machines					
Haemonetics	6 (42.8)	16 (17.4)	22 (20.8)	27.3	3.56 (1.08-11.68)
Fresenius-SN	2 (14.3)	9 (9.8)	11 (10.4)	18.2	1.54 (0.29-7.98)
Fresenius-DN	3 (21.4)	27 (29.4)	30 (28.2)	10.0	0.67 (0.17-2.55)
Amicus-SN	1 (7.2)	13 (14.2)	14 (13.2)	7	0.46 (0.05-3.88)
Amicus-DN	2 (14.3)	27 (29.4)	29 (27.4)	6.8	0.40 (0.08-1.92)
Volume of whole blood processed (L)					
<2.5	4 (28.6)	58 (63.1)	62 (58.5)	6.25	0.23 (0.07-0.80)
>2.5	10 (71.4)	34 (36.9)	44 (41.5)	22.72	4.26 (1.24-14.65)
ACD infusion (ml)					
<250	5 (35.7)	73 (79.4)	78 (73.6)	6.4	0.14 (0.04-0.48)
>250	9 (64.3)	19 (20.6)	28 (26.4)	32.2	6.92 (2.07-23.05)

OR=Odds ratio, CI=Confidence interval, ACD=Acid-citrate-dextrose, SN=Single needle, DN=Double needle

higher in the donor group with ACD infusion more than 250 ml, similar to another author who studied the effect of anticoagulant volume infused and observed that percentage of anticoagulant infused relative to donor's total blood volume was higher for those procedures that resulted in vasovagal reactions.[12] The reason for this could be because of the use of different plateletpheresis machines, type of ACD, rate of ACD infusion, circulating blood volume of donors, continuous or intermittent flow technology, DN or SN, and number of cycles during a collection. Tomita *et al*. also noted that the incidence of reactions increased with increasing cycles during a collection and more volume of ACD was infused to donors. Based on this, they theorized that hypocalcemia may also be involved in the onset of vasovagal reactions in plateletpheresis donors.[11]

Conclusions

The significant predictive factors for donor reactions during plateletpheresis were young (<30 years of age) female donors with low body weight (<60 kg) in which more than 2.5 L volume of whole blood was processed and more than 250 ml of ACD were infused, either on Haemonetics or on Fresenius SN were at increased risk of adverse donor reaction.

The observations in the study are the basis of the following recommendations to reduce adverse donor reactions:

- Careful selection and evaluation of platelet donors by experienced physicians and presence of experienced nurses in donation room, who closely attend the donors during and immediately after donation, play an important role in the prevention of adverse reactions
- Clinically relevant variables that have been identified can and should be used to set protocols to prevent adverse reactions among platelet donors.

In a nation like India where there is a perennial shortage of blood components and the majority of donors are replacement donors, it becomes imperative on our part to make the donation process safe and sound. Overall, platelet usage is likely to increase further, especially because of advances in hematopoietic stem cell transplantation and continued use in coronary artery bypass graft patients, solid organ transplants (liver, lung heart, etc.), dengue epidemic, and trauma. Thus, the care of platelet donors is a continuous process to build up a close link between them and blood center and also to ensure and promote that the donor becomes a voluntary, nonremunerated, regular plateletpheresis donor.

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Conflicts of interest

There are no conflicts of interest.

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